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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/563,683

10/04/2006

Mark T. Gladwin

4239-67618-07

3225

36218 7590 10/15/2008

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EXAMINER

PAGONAKIS, ANNA

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

10/15/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/563,683	<b>Applicant(s)</b> GLADWIN ET AL.	
	<b>Examiner</b> ANNA PAGONAKIS	<b>Art Unit</b> 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 5-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 13-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                            | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)                          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5 sheets, 9/22/2008; 3 sheets, 8/31/2007; 1 sheet, 8/10/2006; 12 sheets, 5/5/2006.</u> | 6) <input type="checkbox"/> Other: _____                          |



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### **DETAILED ACTION**

Applicant's election of hepatic or cardiac or brain ischemia-reperfusion injury in the reply filed on 9/25/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-15 are pending in the application. Claims 5-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Accordingly, no claims have been amended, newly added or cancelled.

This application is the national stage entry of PCT/US04/22232, filed 7/9/2004; and claims benefit of provisional application 60/485,959, filed 7/9/2003 and further claims benefit of provisional application 60/511,244 filed 10/14/2003.

Claims 1-4, 13-15 are currently under examination and are the subject of this Office Action.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1-4, 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (Abstract; J. Cereb. Blood Flow Metab. 1994, 14(2), 217-26) in view of Modin et al (Acta Physiol Scand 2001, 17, 9-16, provided by Applicant).

In the abstract, Zhang et al. teach the use of nitric oxide donors to increase blood flow and reduce brain damage in focal ischemia (title). Zhang et al. teach the nitric oxide donors sodium nitroprusside (3 mg/kg/h) and 3-morpholino-sydnonimide (1.5-6 mg/kg/h) administered into the carotid artery of rats for 60 min. Zhang et al. teach and suggest that nitric oxide donors may represent a new therapeutic strategy for the management of acute stroke.

Modin et al. teach that nitric oxide is derived from nitrite (title). Modin et al. teach that the relaxatory effect of nitrite was increased at pH 6.6 over neutral pH (abstract). Thus Modin et al. teach that non-acidified nitrite also has relaxatory effects similar to "acidified" nitrite (see Figures 1, 2, Figure 4 and respective discussion in text). Modin et al administered various amounts of sodium nitrite but noted a threshold response of 10 microM and near relaxation to basal tone at 1000 microM for the non-acidified sodium nitrite (page 11, Results). Modin et al. teach additional additional agents (ascorbic acid) to enhance the effect of the sodium nitrite (abstract). Modin et al in clued that inorganic nitrite evokes vasodilation most likely through nitric oxide release and that this effect is increased if the pH of the environment is reduced to levels normally found in tissues during ischemia/hypoxia (page 15, last paragraph).

The difference between the instant application and Zhang et al. is that Zhang et al. do not expressly teach non-acidified sodium nitrite in the amount of 0.6 to 240 microM. These deficiency in Zhang et al is cured by the teachings of Modin et al.

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to use non-acidified sodium nitrite within the range instantly claimed, as suggested by Modin et al., in the method of Zhang et al and produce the instant invention.

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One of ordinary skill in the art would have been motivated to do this because Zhang et al. suggest using other nitric oxide donors and Modin et al suggest how much sodium nitrite would be beneficial in tissues during ischemia. Modin et al teach carotid injection over 60 minutes of the sodium nitrite and other forms of administration such as parental, oral, buccal, rectal, ex vivo, or intraocular, peritoneal, intravenous, intraarterial, subcutaneous, inhaled, intramuscular, or cardiopulmonary bypass circuit modes of administration are not only obvious to one of ordinary skill in the art of medicine but also merely result in the same thing; increasing the blood plasma levels of sodium nitrite, in the absence of evidence to the contrary. It is the Examiner's position that rats render obvious other mammals such as humans to one of ordinary skill in the art of medicine.

The concept of treating cerebral ischemia with nitric oxide donors to induce vasodilation and/or increase blood flow is established in the art. Non-acidified sodium nitrite is known to a nitric oxide donor in the art. Applicant has merely followed the suggestions of Zhang et al and Modin et al to use sodium nitrite in the treatment of cerebral ischemia. The predictable expected result is induced vasodilation and increased blood flow in the subject.

From recent case law: "the results of ordinary innovation are not the subject of exclusive rights under the patent laws." (KSR INTERNATIONAL CO. v. TELEFLEX INC. ET AL. 550 U.S. \_\_\_\_ (2007) page 24).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings (In re Opprecht 12 USPQ 2d 1235, 1236 (Fed. Cir. 1989); In re Bode 193 USPQ 12 (CCPA) 1976).

In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a

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whole was *prima facie* obvious to one of ordinary skill in the art at the time of the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 13-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6-13 and 20-23 of copending Application No. 10/563,682. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the instant invention embraces or is embraced by the subject matter of the copending application. One of ordinary skill in the art would recognize the methods in the copending application of treating cerebral ischemia by decreasing blood pressure or increasing vasodilation with a non-acidified sodium nitrite to a subject as embracing the subject matter of instant claims 1-4, 13-15. The same concentrations of sodium nitrite are claimed as well as the subjects and routes of administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Conclusion**

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/  
Supervisory Patent Examiner, Art Unit 1614